Pending Claims

Claims 1 and 21-25 are pending in the application. Claim 26 has been canceled without prejudice; Applicant reserves the right to pursue the subject matter of claim 26 in a related application.

37 CFR § 1.821-1.825

The Office Action states that the specification does not comply with the rules for nucleotide sequence disclosures. Applicant has complied with this requirement by submission of an Amendment and Sequence Listing on January 21, 1998.

Double Patenting

Claim 26 was provisionally rejected as claiming the same invention as that of claim 26 of USSN 08/311,157. This rejection has been obviated by cancellation of claim 26 in this application.

35 U.S.C. § 112, ¶ 1

Claims 21-25 were rejected for alleged lack of enablement. The rejection is based on the belief that:

> While the [previously-filed] declaration demonstrates that baculovirus can be used to transiently express exogenous genes in a variety of cell types by *in vivo* administration, it does not show that one skilled in the art would be able to obtain a significant therapeutic benefit from such expression without undue experimentation.... [S]ustained, high-level expression of introduced genes ... is not routinely obtainable. [Office Action, pg. 3.]

Applicant submits the enclosed Declaration of Dr. James Barsoum as further evidence that baculovirus-mediated gene expression can be used to obtain a significant therapeutic benefit *in vivo* that is sustained over time.

Using art-accepted animal models of human colon cancer (¶¶ 3-6) and human breast cancer (¶¶ 7-12), Dr. Barsoum showed that baculovirus-mediated expression of human interferon-β (hIFNβ) inhibited the formation of tumors and caused tumors to regress in size. The therapeutic effect of a single injection of baculovirus expressing hIFNβ into tumor-bearing mice was sustained for at least 3 months (see ¶ 6). Likewise, a single *ex vivo* treatment of cancer cells with baculovirus expressing hIFNβ was therapeutically effective for at least six weeks after subsequent implantation of the cancer cells into mice (see ¶ 12). These data show that baculoviruses can be used, as described in the specification, to direct exogenous gene expression and obtain a significant and sustained therapeutic effect. In view of the data set forth in the accompanying Declaration of Dr. James Barsoum, along with the Declaration of Dr. Frederick M. Boyce, filed October 8, 1997, and the extensive guidance and data set forth in the specification, Applicant respectfully submits that the rejection for alleged lack of enablement should be withdrawn.

On a final note, Applicant wishes to address a statement in the Office Action referring to the Boyce et al. publication, Proc. Natl. Acad. Sci. vol. 93, pg. 2348-2352 (1996). The Boyce reference stated, and the Office Action quoted:

> Much more work will be necessary to evaluate the safety and efficacy of AcMNPV as a tool for human gene therapy.

Based on this statement, the Examiner concluded that "[s]ince this was published 18 months after the effective filing date of the instant application, any argument that the specification was enabling at the time the invention was made is not persuasive" (Office Action, page 3).

Applicant respectfully submits that there is no legal or scientific basis for concluding that, in view of this quotation, the specification could not be considered enabling as of its filing date. The test for whether a disclosure meets the enablement requirement is:

> whether that disclosure, when filed, contained sufficient information regarding the subject matter of the claims as to enable one skilled in the pertinent art to make and use the claimed invention. [MPEP 2164.01.]

In this case, the record as a whole indicates that the initially-filed disclosure <u>is</u> sufficient to enable one of ordinary skill in the art to make and use the invention. In this case, the specification, the accompanying Declaration of Dr. James Barsoum,[1] and the previously-filed Declaration of Dr. Frederick M. Boyce, overwhelmingly show that the invention can be practiced as initially disclosed without undue

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[1] An Applicant responding to a lack of enablement rejection is <u>not</u> precluded from providing a declaration <u>after the filing date</u> which demonstrates that the invention works as disclosed in the application. MPEP 2164.05.

experimentation. Applicant's evidence far outweighs any negative inference that might be drawn from the statement in the Boyce reference.

The statement quoted from the Boyce reference does not contravene the assertions and evidence on the record. In fact, the authors concluded that:

> [O]ur studies clearly demonstrate that a nonanimal virus may be used as a shell for delivery of nucleic acids to animal cells. [Boyce et al. at page 2352.]

The authors merely acknowledge that further work is necessary to evaluate the safety and efficacy of baculoviruses as a tool for human gene therapy. This statement cannot fairly be read as meaning that the specification does not comply with 35 U.S.C. §112, ¶1. It is well accepted - and even expected - in patent law that further research and development may be warranted before a drug is administered to humans. *In re Brana*, 34 USPQ2d 1436 (Fed. Cir. 1995). The desire for further research before administering a drug to humans does not, however, preclude compliance with 35 U.S.C. §112, ¶1. *Brana* at 1442. In overturning a lack of enablement rejection issued in the absence of human data, the *Brana* court noted:

> Testing for the full safety and effectiveness of [an invention] is more properly left to the Food and Drug Administration (FDA). **Title 35 does not demand that such human testing occur within the confines of Patent and Trademark Office (PTO) proceedings.** [*Brana* at 1442; emphasis added.]

Thus, compliance with the enablement requirement does not turn on the presence or absence of human data.

When the record is viewed as a whole, as is mandated by MPEP 2164.05, it is clear that the initially-filed disclosure is sufficient to enable one to practice the claimed invention without undue experimentation. The sufficiency of this disclosure is exemplified by the experiments set forth in the accompanying Declaration of Dr. James Barsoum, the previously-filed Declaration of Dr. Frederick M. Boyce, and the specification, all of which were carried out in accordance with the guidance provided in the specification. In view of the above, Applicant respectfully requests that this rejection be withdrawn.

CONCLUSION

Applicant submits that all of the claims are now in condition for allowance, which action is requested. Filed herewith is a Petition for Automatic Extension with the required fee.

Please charge any additional fees, or make any credits, to Deposit Account No. 06-1050.

Respectfully submitted,

Date: June 17, 1998

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